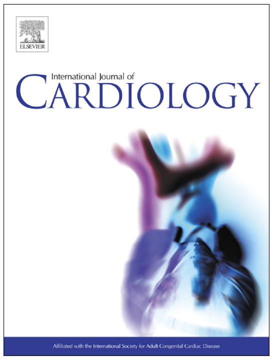

An evaluation of the role of the exercise training dose for changes in exercise capacity following a standard cardiac rehabilitation program

Danilo Iannetta, Codie R. Rouleau, Daniele Chirico, Federico Y. Fontana, Trina Hauer, Stephen B. Wilton, Sandeep Aggarwal, Leslie D. Austford, Ross Arena, Juan M. Murias

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Title:

An evaluation of the role of the exercise training dose for changes in exercise capacity following a standard cardiac rehabilitation program.

Authors:

Danilo Iannetta, PhD[1], Codie R. Rouleau, PhD[2,4], Daniele Chirico, PhD[1,4], Federico Y. Fontana, PhD[5], Trina Hauer[3,4], Stephen B. Wilton, MD[4,6], Sandeep Aggarwal, MD[4,7], Leslie D. Austford[4], Ross Arena, PhD[4,8], Juan M. Murias, PhD[1]

Authors affiliations:

[1]Faculty of Kinesiology, University of Calgary, Calgary, Canada

[2]Department of Psychology, University of Calgary, Calgary, Canada

[3]TotalCardiology™ Rehabilitation, Calgary, Canada

[4]TotalCardiology™ Research Network, Calgary, Canada

[5]Department of Diabetes, Endocrinology, Nutritional Medicine and Metabolism, Bern University Hospital, University of Bern, Bern, Switzerland.

[6]Libin Cardiovascular Institute, University of Calgary, Calgary, Canada

[7]Department of Cardiac Science, University of Calgary, Calgary, Canada

[8]Department of Physical Therapy, University of Illinois at Chicago, Chicago, Illinois, USA

Reprints and correspondence:

Juan M. Murias
Faculty of Kinesiology,
University of Calgary,
KNB 434, 2500 University Drive NW,
Calgary, AB, Canada, T2N 1N4
Email: jmmurias@ucalgary.ca
Phone number: +1 403-220-7955

Abstract

Background: To retrospectively characterize and compare the dose of exercise training (ET) within a large cohort of patients demonstrating different levels of improvement in exercise capacity following a cardiac rehabilitation (CR) program.

Methods: A total of 2,310 patients who completed a 12-week, center-based, guidelines-informed CR program between January 2018 and December 2019 were included in the analysis. Peak metabolic equivalents (MET_{peak}) were determined pre- and post-CR during which total duration (ET time) and intensity [percent of heart rate peak ($\%HR_{peak}$)] of supervised ET were also obtained. Training responsiveness was quantified on the basis of changes in MET_{peak} from pre- to post-CR. A cluster analysis was performed to identity clusters demonstrating discrete levels of responsiveness (i.e., *negative, low, moderate, high*, and *very-high*). These were compared for several baseline and ET-derived variables which were also included in a multivariable linear regression model.

Results: At pre-CR, baseline MET_{peak} was progressively lower with greater training responsiveness ($F_{(4,2305)}$=44.2, $P<0.01$, η^2_p=0.71). Likewise, average training duration ($F_{(4,2305)}$=10.7 $P<0.01$, η^2_p=0.02) and $\%HR_{peak}$ ($F_{(4,2305)}$=25.1 $P<0.01$, η^2_p=0.042) quantified during onsite ET sessions were progressively greater with greater training responsiveness. The multivariable linear regression model confirmed that baseline MET_{peak}, training duration and intensity during ET, BMI, and age ($P<0.001$) were significant predictors of MET_{peak} post-CR.

Conclusions: Along with baseline MET_{peak}, delta BMI, and age, the dose of ET (i.e., training duration and intensity) predicts MET_{peak} at the conclusion of CR. A re-evaluation of current approaches for exercise intensity prescription is recommended to extend the benefits of completing CR to all patients.

Keywords: Exercise intensity; exercise duration; peak MET; cardiorespiratory fitness.

Abbreviations

$\%HR_{peak}$	Percent of peak heart rate
BMI	Body mass index
CR	Cardiac rehabilitation
CRF	Cardiorespiratory fitness
CVD	Cardiovascular disease
ET	Exercise training
GXT	Graded exercise test
HR	Heart rate
HR_{peak}	Peak heart rate
MET	Metabolic equivalent
MET_{peak}	Peak metabolic equivalent

Introduction

The main goal of aerobic exercise training (ET) as an integral component of traditional cardiac rehabilitation (CR) programs is to increase exercise capacity and, thus, cardiorespiratory fitness (CRF) [1], which is the strongest predictor of all-cause and cardiovascular disease (CVD)-related mortality [2,3]. Evidence collected over the years suggests that the group mean improvement in exercise capacity following a standard CR program is on the order of 1.5 metabolic equivalents (MET) (~3-4 $ml \cdot kg^{-1} \cdot min^{-1}$ of O_2 uptake)[4]. However, despite its efficacy at the group level, CR fails to increase CRF in up to 1/3 of patients with CVD [5–7]. This is problematic because failure to increase CRF is associated with a ~30% greater risk of mortality [8,9].

Which patients manifest the greatest benefits in terms of exercise capacity from CR participation is presently unclear. Some reports suggest that patients with lower baseline exercise capacity are the ones improving the most following CR [4,8]; however, this is not a universal finding [10]. An additional factor proposed to modulate CRF during traditional CR programs, yet under-investigated in large cohorts of patients with CVD, is the dose of ET [7,11,12]. In the last couple of decades, several studies in healthy individuals have documented that increasing either the total duration [13] or relative intensity [14,15] of ET can reduce, or even abolish, the incidence of the so-called “*non-responders*” to ET. In CR settings, randomized controlled trials have shown that patients with CVD completing high intensity interval training (HIIT) typically, but not always [16], manifest greater improvements than those completing moderate-intensity continuous training in spite of similar baseline CRF [17,18]. Thus, considering the growing interest towards more personalized approaches for exercise prescription in CR settings [19–21], understanding whether and to what extent the dose of ET modulates changes in exercise capacity is critical to aid with the identification of strategies to maximize the beneficial effects of CR in patients with CVD. Therefore, by retrospectively analyzing a large cohort of patients who completed a 12-week, center-based, guidelines-informed CR program and in whom training and intensity were quantified, we explored whether the dose of ET would be different across different levels of training responsiveness and, thus, whether it would contribute to predict CRF following completion of CR. We tested the hypothesis that, in addition to baseline exercise capacity, greater doses of ET during a standard CR program would lead to greater improvements in exercise capacity.

Methods

Study cohort

A retrospective analysis was conducted on data from patients completing a center-based, guidelines-informed CR program between January 2018 and December 2019 at the TotalCardiology™ Rehabilitation (TC-R) clinic in Calgary, Canada. Patients were included in the analysis if they had *i*) a documented diagnosis of CVD, *ii*) completed at least 40% (≥10 sessions) of the total number of supervised ET sessions [22], and *iii*) successfully completed a graded exercise test (GXT) at pre- and post ET (i.e., GXT terminated due to attainment of maximal effort as deemed by the health professionals administering the test). The study was approved by the Conjoint Health Research Ethic Board at the University of Calgary.

Cardiac rehabilitation program

Details regarding the CR program can be found elsewhere [8]. Briefly, the CR program encompassed a 12-week multidisciplinary approach, during which patients completed medical screening, health behavior counselling, and ET. At pre- and post-ET, patients completed a comprehensive assessment which included physical and anthropometric examinations, a GXT, and blood sample collection for lipid profiles. The symptom-limited GXT was performed within one week before and after the start and the end of the ET phase, respectively, on a treadmill (modified Bruce's protocol) following current recommendations [23,24]. Patients were encouraged to exercise for as long as they could until reaching their maximum level of tolerance. At the moment of exercise termination, the health professionals supervising the GXT (i.e., cardiologists, nurses, and/or exercise physiologists) would record the highest speed/grade, HR_{peak}, and subjective ratings of perceptions attained. For all GXT, HR data were recorded using a wireless 12-lead electrocardiogram system (PC-ECG 1200, Norav Medical, Israel). Peak MET values (MET_{peak}) at the end of the GXT were estimated from the speed and grade of last stage completed using conventional predictive equations [25]. The ET program was 12-week long with sessions performed twice a week. ET sessions were supervised by one health professional and were structured as follows: a 5-min warm-up, 20-60 min of continuous aerobic exercise (e.g., walking, elliptical, or cycling exercise) at an intensity of 60-90% of HR_{peak} (HR; HR_{peak}) measured during the GXT, and a 5-min cool-down. During each session, patients wore a HR monitor (Polar H10, Kempele, Finland), and were instructed to exercise at the pre-established MET values that would elicit the target HR response [4]. Session attendance was recorded upon arrival to the clinic while the duration and the average HR was recorded by the health professionals supervising the ET session who, thereafter, uploaded the information to each patient's electronic medical record. Aside from ET-based components, patients were also offered multidisciplinary support with risk factor management from a dietician, psychologist, exercise professionals, registered nurses, and physicians. After the 12-week period, patients were given instructions on how to continue to implement life-style changes at home, including an exercise program and dietary advice.

Data and Statistical Analyses

Training responsiveness was computed on the basis of changes in MET_{peak} measured at pre- and post-CR. Patients were stratified in different categories based on their level of training responsiveness (i.e., change in MET_{peak}) using a cluster analysis which permits the identification, within a given cohort, of subgroups of individuals sharing similar features (i.e., herein changes in MET_{peak}). In other words, these subgroups represent the optimum clustering solution that minimizes the error sum of squares [26]. Briefly, the first stage of this analysis involved a hierarchical cluster approach using Ward's linkage method with standard Euclidean distance to automatically determine the number of clusters in the data while considering a delta of 1 MET as a minimum meaningful change between clusters [26]. The second stage involved a *k* means non-hierarchical cluster approach to define the most appropriate cluster solution from the previous stage [27]. The five different clusters (or levels) of responsiveness identified by these analyses were: *i*) *negative*; *ii*) *low*; *iii*) *moderate*; *iv*) *high*; and *v*) *very-high*.

To characterize the dose of ET, training duration was computed from summing the overall exercise time (excluding warm up and cool down) during each exercise session. Exercise intensity corresponded to the average %HR_{peak} sustained across all sessions.

Continuous and categorical variables within each cluster of responsiveness were summarized as mean (± standard deviation) and percent (%) frequency, respectively. Comparisons between clusters for continuous (across groups and timepoints) and categorical variables were made using analysis of variance (ANOVA) and chi ($\chi 2$) statistics, respectively. After assumptions verification, to investigate the influence of the dose of ET on peak METs measured at post-CR, a hierarchical multiple general linear model was used to establish relationships between MET_{peak} measured at post-CR with training duration and intensity as well as additional available predictors (i.e., MET_{peak} pre-CR, age, sex, BMI). A $p = 0.05$ level defined sensible predictors within the full initial model. Statistical analyses were conducted with the SPSS software (SPSS, version 29, Chicago, Illinois). Statistical significance was declared when ☐ < 0.05.

Results

Within the time window of interest, 5,795 patients began the center-based CR program. Of these, 2,310 (1,852 [80.2%] males; age 63.0±10.7 years) met the inclusion criteria and, thus, were included in the analyses. When separated for clusters of responsiveness (i.e., *negative*; *low*; *moderate*; *high*; and *very-high*), there were no differences for sex, age, and smoking history frequencies, nor for lipid profiles (*P>0.05*; **Table 1**).

At pre-CR, average MET_{peak} for the entire cohort was 6.9±2.1. Average change from pre- to post-CR was 1.1±1.0 METs ($t_{(2309)} = 50.1$, $P<0.001$; $d = 1.1$). The individual distribution of exercise capacity changes from pre- to post-CR is displayed in **Figure 1** (panel A). **Table 2** displays the physiological and anthropometric outcomes stratified by clusters of responsiveness. At pre-CR, MET_{peak} differed across the different clusters ($F_{(4,2305)} = 44.2$, $P<0.01$, $\eta^2_p = 0.71$) whereby it was the highest in the *negative* cluster, and progressively lower with greater levels of responsiveness. There were no differences for body mass, BMI, waist circumference, rest DBP and SBP across clusters ($P>0.05$). However, there were significant differences across clusters for HR_{peak} ($F_{(4,2305)} = 10.1$, $P<0.01$, $\eta^2_p = 0.17$) whereby it was greater within the *negative*, *low*, and *moderate* clusters as compared to *very-high*, and within the *negative* and *low* clusters as compared to *high*. The average change in MET_{peak} from pre- to post-CR for the *negative, low, moderate, high,* and *very-high* clusters were -0.2±0.5, 0.6±0.1, 1.6±0.3, 2.5±0.2, and 3.6±0.5 METs, respectively. At post-CR, MET_{peak} was greater ($F_{(4,2305)} = 36.3$, $P<0.01$, $\eta^2_p = 0.59$) for the *moderate*, *high*, and *very-high* clusters compared to the *low* and *negative*.

For the entire cohort, average attendance, session duration, and total exercise duration were: 19.0±4.8 sessions, 42.7±11.7 min, and 807.9±266.0 min, respectively. The average HR across all sessions was 99±15 bpm which corresponded to 81.5±9.0% of HR_{peak} measured during the GXT. The box plots of **Figure 1** (panels B, C, and D) display the average attendance, training duration, and $\%HR_{peak}$ across the different clusters of responsiveness. Overall, there were significant differences for total ET duration ($F_{(4,2305)} = 10.7$ $P<0.01$, $\eta^2_p = 0.02$) whereby it was greater within the *low, moderate, high, very-high*, clusters as compared to the *negative* ($P<0.001$). Furthermore, total duration was also greater within the *high* and *very-high* clusters as compared to the *low* ($P<0.001$). In terms of exercise intensity, there were no differences in absolute HR between clusters ($P=0.659$). However, there were difference in $\%HR_{peak}$ ($F_{(4,2305)} = 25.1$ $P<0.01$, $\eta^2_p = 0.042$) whereby $\%HR_{peak}$ within the *moderate*, *high*, and *very-high* clusters was greater compared to the *negative* and *low* ($P<0.001$). Furthermore, the

$\%HR_{peak}$ was also greater within the *high* and *very-high* clusters as compared to the *moderate* ($P<0.001$).

The multivariable regression model (intercept=1.319, CI=0.761-1.876; $P<0.001$) confirmed that both training duration (min) (β=0.001, CI=0.001-0.001; $P<0.001$) and intensity ($\%HR_{peak}$) (β=0.013, CI=0.008-0.017; $P<0.001$) were significant predictors of MET_{peak} post-CR in addition to age (β=-0.014, CI=-0.018--0.010; $P<0.001$), MET_{peak} pre-CR (β=0.860, CI=0.839-0.881; $P<0.001$), and delta BMI (β=-0.103, CI=-0.130--0.075) $P<0.001$).

Discussion

The main aim of this investigation was to identify exercise-based predictors of training responsiveness in a large cohort of patients (n=2310) completing a center-based, guidelines-informed CR program. As hypothesized, baseline MET$_{peak}$ was the strongest predictor of training responsiveness (i.e., patients with lowest exercise capacity demonstrated the greatest changes). In addition to this, and according to our hypothesis, training duration and intensity were also significant predictors of MET$_{peak}$ post-CR. However, it must be considered that.in line with previous reports, improvements in exercise capacity were absent, or low, in almost half of the patients completing the CR program. To our knowledge, the current cohort is the largest analyzed within this important area of research, lending to the strength and impact of our findings. Taken together, these findings highlight the clinical relevance of optimizing the dose of ET (i.e., total duration and intensity) to maximize improvements in exercise capacity especially in those patients who enter CR with the highest baseline exercise capacity.

In recent years, it has become clear that the magnitude of changes in exercise capacity following CR is highly variable between patients [19]. Thus, elucidating the reasons for such a large variability in training responsiveness has been the focus of numerous investigations [4–7,28]. Although not unanimous [10], some studies identified baseline CRF as the most important predictor of CRF post-CR [4,8]. Our study confirms this previous evidence by showing that patients who are more functionally impaired (<5 MET$_{peak}$) at the beginning of CR are those gaining the greatest benefit from it as they demonstrated the greatest changes in exercise capacity (e.g., *high* and *very-high* clusters of responsiveness; **Table 2**). The general consensus as to why baseline CRF is such an important predictive factor revolves around the notion that low-CRF patients may have more opportunities for improvements likely due to a combination of greater sensitivities to the physiological stimulus imposed by ET [4] and progressive mitigations of the central/peripheral cardiovascular derangements over the course of the CR program [29]. In addition to this, the present study indicates that the dose of ET differs remarkably across levels of responsiveness, both in relation to total duration and intensity of ET (**Figure 1**, panels B, C, and D). For instance, the *high* and *very-high* clusters of responsiveness were characterized by a ~15-20% greater training duration (resulting from both greater session attendance and duration) and a ~5% greater relative intensity (in terms of %HR_{peak}) compared to the *negative* and *low* clusters of responsiveness (**Figure 1**, panels B, C, and D). For the entire sample, the multivariable linear regression model confirmed that both training duration and intensity were significant predictors of CRF post-CR. As such, although baseline MET_{peak} remains a key factor predicting changes following CR, our data would also indicate that the dose of ET plays an important modulatory role. Notably, these patterns emerge despite the inclusion of a large cohort of patients in whom the effects of slight differences in the dose of ET may be blunted by differences in CVD prognoses and their severity.

The reasons why patients with a higher CRF at the start of CR accumulated less training duration and exercised at lower exercise intensity during the program, and why this pattern was reversed in patients with the lowest CRF is unclear. Attendance to CR, which is the main factor influencing the computation of training duration, may have been lower due to multiple factors including social, financial, and psychological reasons [30,31]. On the other hand, lower levels of intensity during CR may have stemmed primarily from reduced patient motivation, increased fear of reoccurring cardiac events, and/or from an overly conservative exercise intensity prescription [6,32,33].

Making the case for optimizing exercise prescription in patients with the highest baseline CRF

What emerges clearly from the present dataset, which was composed by patients who completed a center-based CR program, is that those who are the most fit at the beginning of CR are more likely to demonstrate the lowest gains in exercise capacity at the end of it. Considering the importance of improving CRF across all patients with CVD [8,9], and that such an improvement may also be associated with other favorable changes in additional modifiable risk factors (e.g., BMI; **Table 2**) [34], the present findings highlight the importance of extending the benefits of CR to patients demonstrating a high MET_{peak} at the beginning of CR who, paradoxically, risk ending it with lowest MET_{peak}. Although the presence of a ceiling effect cannot be excluded, the matter of crux most likely lies within a poor attendance and a suboptimal exercise intensity prescription. In this context, although less predictive than in previous studies [35], increasing ET session attendance may be key in these patients to optimize CR outcomes. Furthermore, considering that total energy expenditure of ET seems to be an important driver of positive outcomes [36], adding more ET sessions to those currently offered as part of standard CR programs worldwide may also provide additional benefits. On the other hand, given that small changes in relative exercise intensity can lead to large changes in the physiological stimulus [37], the relative intensity at which ET is sustained is of primary importance [38]. A recent study combining data from patients with CVD collected by multiple clinics demonstrated that the first ventilatory threshold, which represents an important boundary separating intensities with no metabolic perturbations (i.e., moderate) from those with markedly greater perturbations (i.e., heavy) [39], occurred at ~80% of HR_{peak} [40]. Interestingly, in the present study, we observed that average exercise intensity within the *negative* and *low* clusters of responsiveness corresponded to a similar $\%HR_{peak}$ (i.e., 79.6% and 80.5%, respectively; **Figure 1**, panels D). Given that this boundary presumably demarcates the minimum intensity to surpass in order to engender a meaningful physiological stimulus in patients with CVD [20], it could be speculated that intensity of ET for many of the patients within these clusters might have been too low. This observation is line with the recent widespread consensus [20,32,37,41–45] on the necessity of re-evaluating current methods for exercise intensity prescription to implement more personalized and goal-oriented methods.

Exercise and capacity and weight loss.

Weight loss continues to be a challenge in patients participating in a traditional CR program. Traditional CR programs rarely include a distinct weight loss component, beyond a general emphasis on increasing physical activity and heart-healthy nutrition, resulting in negligible effects on BMI [46]. This is surprising, given that the average BMI of patients referred to CR is ~30 kg/m^2 (e.g., **Table 2** herein) and obesity is an important risk factor for several CVD [34]. Our findings demonstrate a reduction in body mass and BMI from pre- to post-CR within the *moderate*, *high*, and *very-high* clusters whereas the *negative* cluster demonstrated an increase in body mass. Although no directionality/causality can be inferred from the present data set, the exercise capacity-to-weight loss relationship demonstrated herein warrants further investigation.

Limitations

The major strength of this investigation is the inclusion of a large cohort of patients in whom we obtained data during ET in real-world clinical practice. However, there are some limitations that need to be acknowledged in order to delimitate our interpretations. First, our analysis of training responsiveness was focused solely on changes in exercise capacity (i.e., MET$_{peak}$). However, we want to emphasize that other benefits can be gained from participation in a multidisciplinary CR program, such as smoking cessation, sleep and dietary improvements, stress reduction, etc. [47,48] and that these can greatly contribute to enhance patients' quality of life. Secondly, although the GXT was performed according to standard guidelines [23,24] and carried to each patient's perceptual limit, we cannot exclude the possibility that in some patients such limit did not correspond to their maximum attainable exercise level. Such a possibility could have affected the magnitude of the pre- to post-CR changes in MET$_{peak}$ and the accuracy by which relative intensity (on the basis of HR) was quantified and interpreted. Thirdly, the computation of the dose of ET was based solely on the supervised sessions completed at the clinic; thus, it is unknown to what extent physical activity performed in addition to ET offered by the clinic may have been of importance to explain our findings. Fourthly, in line with previous studies of ours [4,8] and with the fact that referrals of females patients to CR are generally lower compared to males [49], our sample had a greater proportion of males. Thus, although sex did not contribute significantly to our findings, its potential modulatory role cannot be excluded [6] and should be considered in future investigations. Finally, interpretations in relation to CRF are inferred from the measure of exercise capacity obtained at the of the GXT, as respiratory data were not available. However, considering the proportionality between exercise-estimated and respiratory-measured CRF [25] and that training responsiveness remains highly variable even when CRF is directly measured [6,7], there is confidence that the changes in MET_{peak} observed herein reflect changes in CRF and that our conclusions would have not differed if CRF was measured instead of estimated.

Conclusions

With the goal of optimizing exercise training prescription in CR settings, there has been a growing interest in pinpointing the factors contributing to changes in CRF over the course of CR programs [19]. The current study contributes to this body of literature by showing, in a large cohort of patients with CVD, that baseline MET_{peak} is the strongest predictor of training responsiveness and that progressively greater levels are associated with greater doses of ET. Although more studies are needed to continue unveiling the true contribution of ET in CR settings, the present study highlights that a more tailored exercise prescription might be needed to maximize the outcomes of current supervised CR programs especially in patients less functionally impaired at the beginning of the CR program.

Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

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Table 1. Baseline characteristics of patients included in the study (total n=2310).

	Level of responsiveness to ET					
Characteristic	**Negative n=473**	**Low n=670**	**Moderate n=914**	**High n=159**	**Very-high n=94**	***P* value**
Sex, *%*						
Males	78.2	78.4	82.5	81.1	78.7	*0.212*
Age, *years* (*SD*)	64 (11)	62 (11)	63 (10)	63 (11)	63 (11)	*0.151*
Primary referral reason, *%*	30.2	28.8	25.9	23.9	17.0	*0.047*
IHD	21.4	18.7	21.7	14.5	20.2	*<0.001*
NSTEMI	19.5	22.8	27.9	34.0	33.0	*<0.001*
STEMI	29.0	29.7	24.5	27.7	29.8	*0.165*
Other						
Diabetes, *%*	21.4	18.1	17.3	23.3	21.3	*0.169*
Medication use, *%*						
ARBs	21.4	21.6	16.8	15.1	16.0	*0.062*
DOACs	10.4	8.5	9.5	8.8	9.6	*0.724*
APA P2Y12	63.4	64.0	67.2	61.6	67.0	*0.401*
β-blockers	79.3	79.7	81.6	84.3	80.9	*0.540*
CCBs	18.2	12.4	14.1	11.9	10.6	*0.044*
TZDs	21.4	18.1	17.3	23.3	21.3	*0.252*
Smoking status, *%*						
Never Smoked	45.7	49.6	46.7	50.3	47.9	*.646*
Quit > 6 months	40.2	38.5	41.2	40.9	37.2	*.814*
Quit < 6 months	9.1	9.1	8.9	5.7	11.7	*.553*
Current smoker	5.1	2.8	3.2	3.1	3.2	*.313*
Blood risk factors (*SD*)						
HDL, mmol/L	1.11 (0.32)	1.11 (0.32)	1.08 (0.32)	1.12 (0.36)	1.12 (0.32)	*0.514*
LDL, mmol/L	1.98 (1.03)	2.08 (1.04)	2.04 (1.02)	2.04 (1.04)	2.08 (1.00)	*0.686*
Total Cholesterol	3.84 (1.16)	3.93 (1.21)	3.86 (1.19)	3.83 (1.15)	3.87 (1.18)	*0.787*
Triglycerides	1.80 (1.48)	1.64 (0.92)	1.68 (1.33)	1.49 (0.81)	1.54 (1.01)	*0.069*

Overall differences across groups were determined by analysis of variance or χ^2.
IHD, ischemic heart disease; NSTEMI, Non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; ARBs, angiotensin II receptor blockers; DOACs, direct oral anticoagulant; APA P2Y12, antiplatelet P2Y12 inhibitor; CCBs, calcium channel blockers; TZDs, thiazolidinediones; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Table 2. Physiological and anthropometric changes from pre- to post-CR (total n=2310).

Variable	Level of responsiveness to ET Negative n=473	Low n=670	Moderate n=914	High n=159	Very-high n=94	*P* value Groups	Time/ Groups
MET_{peak}							
PRE	7.3 (2.2)	7.2 (2.1)	6.8 (1.9)$^{*\#}$	5.8 (2.0)$^{*\#\&}$	4.8 (1.8)$^{*\#\&\$}$	*<0.001*	*<0.001*
POST	7.0 (2.3)^{a}	7.9 (2.1)^{a}	8.4 (1.9)$^{*\#a}$	8.3 (2.1)$^{*\# a}$	8.4 (8.4)$^{*\#a}$	*<0.001*	
Δ	-0.2 (0.5)	0.6 (0.1)	1.6 (0.3)	2.5 (0.2)	3.6 (0.5)		
Body mass, *kg*							
PRE	85.6 (20.7)	85.4 (18.0)	84.7 (16.2)	84.4 (18.2)	81.1 (18.2)	*0.225*	*<0.001*
POST	85.9 (21.5)^{a}	85.1 (18.0)	83.7 (15.7)^{a}	82.[illegible] (17.7)^{a}	79.8 (17.7)^{*a}	*0.010*	
Δ	0.3 (3.4)	-0.3 (3.5)	-1.0 (3.8)	-1.6 (4.2)	-1.2 (-1.2)		
BMI, *kg/m*^{2}							
PRE	28.6 (5.9)	28.4 (5.0)	28.2 (4.7)	27.8 (5.2)	27.5 (4.8)	*0.152*	*<0.001*
POST	28.7 (6.2)	28.3 (5.1)	27.8 (4.6)^{*a}	27.2 (5.1)^{*a}	27.0 (4.6)^{*a}	*0.001*	
Δ	0.1 (1.5)	-0.1 (1.3)	-0.3 (1.4)	-0.5 (1.4)	-0.5 (1.5)		
Waist, *cm*							
PRE	102 (14)	101 (14)	101 (12)	100 (13)	99 (14)	*0.351*	*<0.001*
POST	101 (15)^{a}	101 (13)^{a}	99 (12)^{*a}	98 (13)^{a}	98 (14)^{a}	*0.002*	
Δ	-1 (5)	0 (5)	-2 (5)	-2 (6)	-2 (6)		
Rest DBP, *mmHg*							
PRE	70 (9)	70 (9)	70 (9)	69 (9)	68 (9)	*0.177*	*0.038*
POST	70 (8)	70 (8)	71 (8)^{a}	70 (8)	71 (9)^{a}	*0.665*	
Δ	0 (9)	0 (9)	1 (10)	1 (10)	3 (10)		
Rest SBP, *mmHg*							
PRE	116 (16)	114 (15)	114 (16)	113 (17)	111 (14)	*0.720*	*0.061*
POST	117 (16)	116 (15)	116 (15)	115 (15)	117 (15)	*0.673*	
Δ	1 (17)	2 (16)	2 (17)	1 (17)	6 (13)		
HR_{peak}, *bpm*							
PRE	126 (22)	125 (22)	123 (21)	118 (21)$^{*\#}$	113 (19)$^{*\#\&}$	*<0.001*	*<0.001*
POST	125 (23)	129 (22)^{*a}	131 (21)^{*a}	132 (21)^{*a}	128 (21)^{a}	*<0.001*	
Δ	0 (14)	4 (14)	9 (15)	14 (16)	15 (16)		

End GXT symptoms, *%*						
Leg Fatigue	17	17	19	18	17	*0.862*
PRE	19	19	18	18	13	*0.650*
POST						
Dyspnea	31	35	36	39	31	*0.171*
PRE	37	31	32	23	27	*0.010*
POST						
General Fatigue	41	37	35	25	37	*0.008*
PRE	28	38	41	49	49	*<0.001*
POST						
Unable to keep	5	5	3	4	3	*0.137*
up	8	6	7	6	7	*0.518*
PRE						
POST	6	6	7	14	12	*<0.001*
Other	8	7	4	4	4	*0.010*
PRE						
POST						

MET_{peak}, peak metabolic equivalent, BMI, body mass index, DBP, diastolic blood pressure, SBP, systolic blood pressure, HR_{peak}, peak heart rate

[*] *Different from Negative*

[#] *Different from Low*

[&] *Different from Moderate*

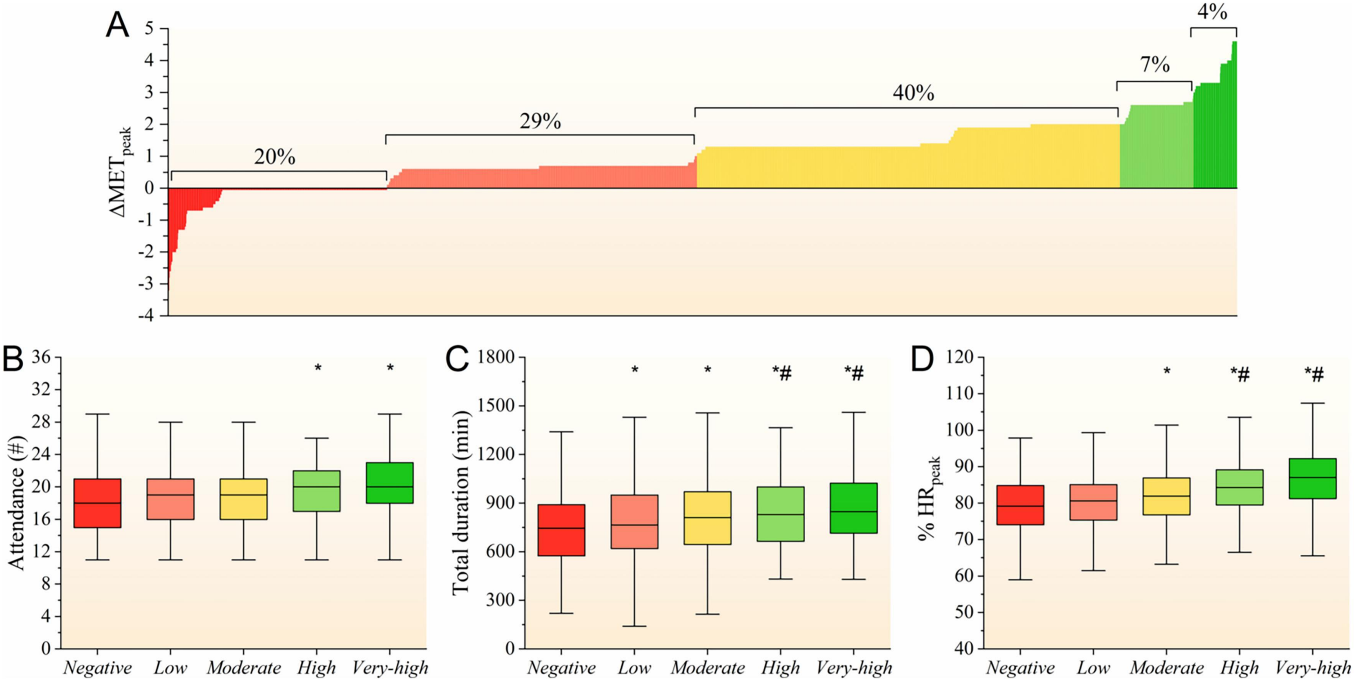
[$] *Different from High*

[a] *Different from PRE within the same cluster*

Figure legend

Figure 1. Panel A displays the distribution of individuals on the basis of changes in exercise capacity (as measured by peak metabolic equivalents (MET$_{peak}$)) during a graded exercise test. Percent values represent the percent number of patients within each identified cluster (i.e., *negative*, *low*, *moderate*, *high*, and *very-high*). The box plots of panels B, C, and D display the cluster-specific distribution of sessions attended, total duration (min), and exercise intensity [% of peak heart rate (%HR$_{peak}$)], respectively, for the 12-week cardiac rehabilitation program. Within each box, horizontal lines denote median values; the confines of each box plot extend from the 25th to the 75th percentile (i.e., interquartile range); whiskers reach to the most extreme values within 1.5 of the interquartile range. * Different from *negative*; # different from *low* ($P<0.05$).

- Exercise training is an integral part of cardiac rehabilitation programs
- Cardiorespiratory improvements following cardiac rehabilitation are variable
- Intensity and total duration of exercise training predict improvements



A
ΔMET_peak
20%
29%
40%
7%
4%
5
4
3
2
1
0
-1
-2
-3
-4
B
Attendance (#)
*
*
C
Total duration (min)
*
*
*#
*#
D
% HR_peak
*
*#
*#
Negative
Low
Moderate
High
Very-high

Figure 1